REMARKS

Claims 1-12 remain in the present application. The Office Action of September 25, 2002, has been carefully studied. It is believed that all of the claims are patentable.

Specification

Trademarks must be capitalized.

The specification has been checked to determine the presence of all possible minor errors. In accordance with the Examiner's suggestion, all readily identifiable trademark shave been capitalized.

Rejections under 35 U.S.C. 112.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification is said to enable methods for determining the level of glucose and hemoglobin in a sample obtained from a hair follicle, saliva, or urine from an individual, the Examiner alleges that the specification does not enable any person skilled in the art to which it pertain to use the invention commensurate in scope with the claims.

This rejection is respectfully traversed. As the Examiner is well aware, there is no requirement that specific examples be provided to enable the invention, if the invention can be practiced without undue experimentation.

There is no reason to believe that one skilled in this art would not be able to analyze the existence of any analyte whose presence in a non-blood sample may attest to its existence in the blood. Submitted herewith as ANNEX A is a compilation of published literature demonstrating the analysis of different analytes, such as drugs of abuse, organic analytes, inorganic analytes, etc., which may be detected in, for example, hair and saliva samples. These assays can be conducted on any non-blood sample which can be analyzed by standard analytical techniques.

On page 4, lines 5-10, the Examiner alleges that "…there is no teaching that the level of analyte found in the sample correlates to the amount of analyte found in the blood of an individual."

With respect to the correlation between concentrations of glucose in hair and in the blood, submitted herewith as ANNEX B are additional experimental examples which were conducted in accordance with the description in the application, and which demonstrate that the level of glucose in hair correlates well with the level of glucose in the blood. Attention is further directed to references **a-e** of ANNEX A, which provides grounds for the correlation. Other references disclose known methods for detecting various other analytes in

hair and saliva samples. The fact that these methods are disclosed is evidence that a correlation between blood concentrations and sample concentrations of specific analytes may indeed be made.

On page 14, lines 11-21 and page 5, lines 1-2 of the Office Action, the Examiner alleges that claim 4 fails to teach how the fractions of blood and interstitial fluid are separated from each other, and that the description in the application fails to teach how one determines the level of blood found in the interstitial fluid.

Applicant agrees with the Examiner that hemoglobin and red blood cells are not normally components of the plasma or of the interstitial fluid. However, the following will clear up this misunderstanding.

Claim 4 reads as follows:

A method according to claim 1, wherein said non-blood sample is a sample of hair contained from said individual, the method comprising:

(i) obtaining a sample of hair from said individual;

(ii) determining the amount of blood or interstitial fluid in said

obtained sample and, if necessary, correcting variations between different hair samples;

(iii) determining the level or concentration of said analyte in said blood or interstitial fluid; and

(iv) calculating the level of said analyte in the [analyte] blood of the tested individual based on the measurements in (i) and (ii).

Claim 4 claims a method of **indirectly** determining the amount of analyte, [e.g., glucose, in the blood of a patient by way of determining the amount of analyte glucose in **either** the interstitial fluid **or** the blood obtained from a hair sample and comparing the amount to the total amount of interstitial fluid **or** blood, **from which the glucose was extracted.**

This method **does not** teach the determination of blood or blood components in the interstitial fluid, nor does it teach the determination of red blood cells in the plasma.

Example 1, Section c, beginning at the bottom of page 17 of the specification, explains the process by which the amount of glucose in either the interstitial fluid or blood is independently determined. One skilled

in the art can readily conduct this determination without undue experimentation.

On page 5, lines 3-19, the Examiner states, "There is no guidance as to what analytes, besides glucose, can be analyzed using this method." However, page 5, second paragraph, of the specification as filed defines "analyte" as "…any substance or component found in the blood, for example, sugars, proteins, organic, compounds, etc.," which is present in detectable amounts in the non-blood fluid sample. It is clear from this that any compound which can be detected in the sample can be the subject of analysis according to the present invention.

On page 5, third paragraph of the Office Action, the Examiner agues that the art teaches away from "…using determined glucose levels in saliva to determine the level of analyte in the blood of a donor" and cites Ben-Aryeh et al., who teach, "…salivary glucose concentrations were not significantly correlated with serum glucose, thereby preventing the use of saliva for monitoring blood sugar."

It should be noted that Ben-Aryeh et al., nor any other researchers, do not teach determining glucose from samples by way of correcting the glucose measurement by the measurement of hemoglobin. This combined method

of the present invention enables correct quantification of glucose in the sample, and therefore, correct quantification of glucose in the blood. Furthermore, there is nothing in Ben-Aryeh et al. relating to determining glucose in the interstitial fluid, which may be separated from the saliva, as in the present invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

This rejection is respectfully traversed. It should be noted that the present invention provides a method for determining the level of an analyte in the blood of an individual using a non-blood sample, and that the specification and claims clearly state each step required in this process. However, the methods for determining the volume of blood in a sample, or the amount of analyte in the sample, are conventional assays, and there is no need to recite specific steps, as one skilled in the art would readily appreciate how these assays would be conducted.

Claims 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

mater which applicant regards as the invention. Claim 4 is said to be unclear as to whether the measurements of hemoglobin and glucose were carried out using a sample which comprises both blood and interstitial fluid.

This rejection is respectfully traversed.

Claim 4 depends from claim 1, namely, a method for determining the level of an analyte in the blood of an individual wherein the non-blood sample is a sample of hair. The method comprises determining the amount of blood or interstitial fluid in the sample and determining the level or concentration of the analyte in the blood or interstitial fluid. In this case, the hair sample may contain blood or interstitial fluid or both. Referring again to claim 1, the method requires determining the volume of blood in the sample, which means the amount of blood in the interstitial fluid, or the amount of blood in the hair.

Claim 9 recites an instrument "capable of" detecting and analyzing a signal, which the Examiner alleges is unclear.

Claim 9 has now been amended in accordance with the Examiner's helpful suggestion.

Prior Art

The prior art made of record and not relied

upon is merely considered to be pertinent to applicant's disclosure.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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"Version with markings to show changes"

IN THE SPECIFICATION

Page 17, please amend the first paragraph beginning on line 1 as follows:

In a micro-centrifuge ("Eppendorf" style) test tube, 25µL of the above sample is mixed with 100µL of a glucose oxidase, horseradish peroxidase mix, prepared from the enzyme capsule in Sigma Chemicals colorimetric glucose test kit (cat # 510-A or 510-DA). Following 10 minutes incubation at room temperature (18-30°C), a hundred µL of 1:1 diluted Pierce (Rockford, IL, USA) ~~PowerSignal™~~POWERSIGNAL™ Luminol/Enhancer (derived from cat # 37075) are then added and incubation continued for another 1 minute. The test tube is then inserted into a Labsystems ~~Luminoskan~~LUMINOSKAN luminometer and the luminescence is recorded.

Page 17, please amend the second paragraph beginning on line 16 as follows:

In a micro-centrifuge ("Eppendorf" style) test tube, 25µL of the above sample is mixed with 100µL of Pierce ~~PowerSignal™~~POWERSIGNAL™ ELISA Chemiluminescent Substrate Working Solution, prepared according to the instructions of product # 37075. Following 1 minute of incubation, the test tube is then inserted into

Labsystems ~~Luminoskan~~LUMINOSKAN luminometer and the luminescence is recorded.

Page 18, please amend the last paragraph beginning on line 25 as follows:

In a micro-centrifuge ("Eppendorf" style) test tube, 25µL of the above sample is mixed with 100µL of a glucose oxidase, horseradish peroxidase mix, prepared from the enzyme capsule in Sigma Chemicals colorimetric glucose test kit (Cat # 510-A or 510-DA). Following 10 minutes incubation at room temperature (18-30°C), a hundred µL of 1:1 diluted Pierce (Rockford, IL, USA) ~~PowerSignal™~~POWERSIGNAL™ Luminol/Enhancer (derived from Cat # 37075) are then added and incubation continued for another 1 minute. The test tube is then inserted into a Labsystems ~~Luminoskan~~LUMINOSKAN luminometer and the luminescence is recorded.

Page 19, please amend the first paragraph beginning on line 6 as follows:

In a micro-centrifuge ("Eppendorf" style) test tube, 25µL of the above sample is mixed with 100µL of Pierce ~~PowerSignal™~~POWERSIGNAL™ ELISA Chemiluminescent Substrate Working Solution, prepared according to the instructions for product # 37075. Following 1 minute of

incubation, the test tube is then inserted into a Labsystems ~~Luminoskan~~LUMINOSKAN luminometer and the luminescence is recorded.

IN THE CLAIMS

9. (Amended) A kit according to claim 6, further comprising a test strip incorporating reagents or structures necessary to carry out the measurement of the tested analyte and blood component and a instrument into which the test strip can be inserted into or to which the test strip may be connected; said instrument ~~capable of detecting and analyzing a signal emitted by said test strips~~being an instrument that detects and analyzes and optionally translating said signals into prevalent units.